

The Bio-Micro Experience

Report on Brainstorming Session, DARPA Microflumes PI Meeting, Tucson, AZ, January 2000
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- **Bio Sciences and Engineering: what are the issues in working together. If the end goal is science versus engineering, what is the difference of approach from the two communities? What have we learned from our multidisciplinary program (what works, what not)?**

It was the consensus that within the DARPA Microflumes "family", most engineers have been "converted" to understanding and dealing with biologists and biologists "converted" to understanding and dealing with engineers. The issue then is really how to bring new folks to this enlightened view.

The following cultural comparisons were noted:

Engineers	Biologists
Are application driven, usually have a goal to make something that works, and often have forgotten what a hypothesis is	Are hypothesis driven, are usually motivated to understand something, and have often forgotten what an application is
Often don't appreciate how many unknown variables exist in almost every biological system; often naïvely believe biological data and publications which are frequently flawed	Often don't trust modeling or theory because they have trouble conceiving of a system in which all relevant variables are controlled; sometimes don't believe things they see with their own eyes
Reproducible= error rate < 1 in 10^9	Reproducible= works 7 out of 10 times
Can usually plan out a realistic project schedule based on rule of thumb ideas of how long it takes to make each part of something work; usually stick to their schedule (+ 15% !)	Have a fuzzy idea of time because seeking understanding and having experimental systems that are almost always ill-defined makes scheduling very hard; sometimes stunned if held to a real schedule
Get excited about making something work reproducibly; consider characterizing something (not necessarily understanding it) a prelim to achieving this	Get excited about understanding something; may consider properly characterizing and making it work reproducibly an unnecessary chore
"Paint" more like Dutch masters	"Paint" more like impressionists

Although these differences are stated stereotypically (and deliberately so for fun) they symbolize two real and deeply held world views (paradigms) that must be bridged when engineers and biologists come together for a project. Otherwise there may be unexpected misunderstandings about what the other side expects, and can and will do. Fortunately there is always a subset of open-minded individuals in each scientific camp. The key is matchmaking these subsets to create successful interdisciplinary teams rather than trying to go on a crusade to convert the unconvertible. Realistic scheduling and the possibility of successful system/assay integration will not be feasible if these cultural gaps are not bridged.

It is important to consider up front how to manage a project if team members will be from different disciplines, especially if they will work in different institutions providing different cultural milieus. It was the consensus that the PI needs to ensure everyone has a shared vision, sets clear goals that are understood and agreed to by all, has a sympathy during the ups and downs of a typical project with the different perspectives, and anticipates that there may be completely different reactions to technical difficulties along the way.

- **The parallel development of "bio" and "microengineering" - should there be a parallel effort to develop microscale-compatible biological agents?**
 - **When a biologist or biochemist develops an assay or a reagent is it necessary to know into which microsystem it will go?**

Most biological reactions occur in or between cells in the fL to pL volume range. When they are used in microflumes, reactions are therefore in some senses closer to their native environment than they are in benchtop reactions. Nevertheless, issues connected with surface compatibilities become important in microflumes because the surface to volume ratio is much greater than in a test tube. Surface coatings may be important but since some biological systems tend to have affinity for hydrophobic surfaces while others have affinity for hydrophilic ones, no universal coating solution seems to be feasible at this stage of our understanding. Flow shear may also be much greater in microflumes than in benchtop fluid handling devices and some biological structures, especially cells, may be inadvertently damaged in microflumes if this is not taken into account. Issues such as mixing are also important because this can be difficult in a microflume and is often taken for granted on the bench. For many such reasons, it is important for biologists and biochemists to discuss new assay systems with microengineers before a design is chosen. It was considered more important to have a dialog than a parallel development path *per se* between assays and microflume engineering, although a parallel path does allow for assays and microflumes to meet face to face periodically for reality checks during development.

- **When a microengineer develops a new microfluidic chip platform is it important to know what assays it will enable?**

This depends upon how general the architecture is for the microflume. Certainly it is possible to create useful microflumes "in a vacuum" if they have applicability to a wide range of fluid manipulations. An approach to this is developing functional blocks to provide a library of solutions that can be independently and thoroughly modeled and then brought together later to form multistage microflumes much in the same way as a library of electronic functional blocks can be used to make complex ICs. On the other hand, when it comes to getting a specific assay optimized, closer interaction between biologists and engineers is desirable. Such interactions open up new avenues: one exciting feature of microflumes is that they enable manipulations of which biologists are generally unaware. Effects like the lack of mixing in parallel laminar flow streams, dielectrophoresis, electrohydrodynamic pumping, and many others only come to the fore on the microscale. These effects tend to be unknown to bio people and will not figure in their thinking at all yet may be very useful in solving microfluidic integration problems. Similarly, there are many biological effects of which engineers are unaware that might similarly be exploited on the microscale. Collaborations allow new and elegant design solutions to emerge; surely this is the value of an interdisciplinary approach.

- **Do the efforts of "bio" and "microengineering" go hand-in-hand? If so, how would you prevent one side from simply "using" the other side?**

It was felt that a shared vision of what constituted success in a project is critical and that it is important for the PI to set goals that approach this vision by providing something for everyone. Thus the vision has to cross the cultural divide between biology and microengineering through both mutually and individually satisfying goals. In this way the vision can provide individual benefits for the participants who, if they are to be content, must perceive some benefits that extend into an "afterlife" - i.e. their own work after the collaboration ends. To achieve this, each side should derive benefit in his or her own field as the project progresses: microengineers should end up with some cool engineering and biologists with some cool biology. Both sides should see some benefits from intellectual property. In this way both sides advance in the forum they know best while gaining the benefit of cross-pollination and crossover publications in the forum to which they are new. This approach should be planned when putting together the project initially because it will ensure that each side can receive peer recognition, a sense of equality, and a sense of mutual satisfaction in the project.